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Diagnosis and Follow Up of Idiopathic Dilatation of Inferior Vena Cava

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Abstract

In the absence of cardiac pathology, the presence of a dilated inferior vena cava (IVC) is considered idiopathic. To date this phenomenon has only been described in athletic individuals as an adaptation to chronically augmented venous return. This is the largest prospective cohort study, following ten individuals with idiopathic dilated IVC against an age matched control group with annual echocardiograms and cardiac magnetic resonance (CMR) imaging for a median of 55 months. No significant difference was found between echocardiography and CMR measurements in IVC diameter assessment both at baseline and at follow up. Over the study period there was no significant progression of the IVC in diameter as measured either by echocardiography or CMR. None of the patients suffered any cardiovascular events and there were no hospitalizations. Our findings indicate the benign nature of this condition and provide reassurance with regards to future clinical implications.

Keywords: Inferior Vena Cava, Echocardiography, Magnetic Resonance Imaging

Introduction

The inferior vena cava (IVC) is a highly compliant vessel that modulates its diameter and cross-sectional area in parallel with changes in blood volume. The IVC is dilated in patients with elevated right atrial pressure, right ventricular hypertrophy, tricuspid valve disease and pericardial constriction reflecting similar and parallel changes in central blood volume and capacitance. Aside from these volume dependent conditions the IVC can also be dilated in otherwise healthy individuals. In the absence of any cardiac pathologic condition, the finding of a dilated IVC is considered primary or idiopathic[1]. The diagnosis of idiopathic dilated IVC is usually a diagnosis of exclusion usually performed by echocardiography and variably supported by additional non cardiac diagnostic tests. Overall, little is known about this condition mainly because it is encountered so infrequently. It is presumed that this vascular dilation maybe the effect of adaptation to chronically augmented venous return from the lower part of the body, causing increased volume load with increased cardiac output [1]. Supporting this theory is that idiopathic dilatation of IVC (IDIVC), is usually encountered in young athletes.

There are several cases of IDIVC that are also found in non-athletic or young and physically active individuals, arguing against a solely volume-related theory. To acquire more understanding of this imaging finding we wished to evaluate consecutive patients with suspected idiopathic dilated IVC with comprehensive multimodality imaging and to serially follow up the IVC dilatation to determine if there is any progression.

Methods

Patient Population

We prospectively evaluated patients with suspected IDIVC initially screened by echocardiography. Eligible patients were identified from those referred to two major inner city tertiary centers for echocardiographic assessment from January 2009 to December 2014. Inclusion criteria were dilated IVC as defined by echocardiography (see below). Exclusion criteria were: echocardiographically assessed significant tricuspid valve disease defined as greater than mild severity, right ventricular dilatation or hypokinesia as defined by the American Society of Echocardiography 2015 chamber quantification guidelines, prior history of cardiac disease, history of thromboembolic disease and pericardial disease. We have also excluded patients with known or suspected liver disease. To exclude concomitant intra-abdominal pathology (whether compressive of functional) as potential cause for venous stasis within the IVC all patients underwent comprehensive abdominal ultrasound and liver enzyme testing.

Eligible patients underwent repeated transthoracic echocardiography and cardiac magnetic resonance at baseline (visit 1) and yearly thereafter.

10 healthy volunteers matched for age and sex constituted the control group. They underwent baseline transthoracic echocardiography and CMR that was then compared to the case group. The study was approved by the local ethics committee.

Echocardiography

All patients underwent echocardiography in the left lateral decubitus position, using commercially available echocardiographic platforms (Philips iE 33, Philips Healthcare, Andover, MA) equipped with 2.5 Hz probe and all echocardiographic data were

subsequently digitally stored. Left atrial and ventricular diastolic diameters (LVDD), interventricular septal and posterior wall thickness (IVSTD and PWTD) were measured according to the guidelines of the American Society of Echocardiography[2]. The left ventricular volumes were measured by biplane 2D Simpson's method. The peak early (E) and late (A) transmitral flow velocities and deceleration time of E velocity were measured; the ratio of early-to-late peak velocities (E/A) was calculated. From tissue Doppler (TDI), the early diastolic (E′) at the septal corner of the mitral valve annulus was measured; the E/E′ ratio was calculated

The patient was then placed in the supine position and the IVC diameter was determined in the long- and short-axis views in the subxiphoid approach 10 to 20 mm away from its junction to the right atrium[3] (Figure 1a). The IVC was described as normal when its median diameter was 1.6 cm, dilated when median diameters were 1.7 to 2.5 cm, and very dilated when it was 2.6 cm or more[4]. This description of the IVC is a conjunction of 2010 American Society of Echocardiography and European Association of Echocardiography recommendations[3]. All measures reflect the median values between maximal inspiratory and expiratory values in 3 consecutive spontaneous respiratory cycles. IVC Doppler flow velocities were obtained in the subxiphoid approach in the hepatic vein near its junction to the IVC[3] (Figure 1b). To assess IVC collapsibility, the phasic respiratory variation of IVC diameter was calculated as follows ($IVC_{max} - IVC_{min}$)/(IVC_{max}) ×100. All echocardiographic measurements took place over the same beats as per guidelines.

Cardiac Magnetic Resonance (CMR)

All patients were evaluated using a 1.5T scanner (Avanto, Siemens, Erlangen Germany). Cine images were obtained for assessment of mass and function using an

SSFP sequence in long-axis planes and short-axis slices from the mitral valve to the apex of the left ventricle as previously described[5]. The IVC was visualized and assessed in two views transverse and sagittal (Figure 2a and 2b respectively). To capture the phasic respiratory changes of IVC SSFP was used as preferred modality. As respiration and changes in intrathoracic and intra-abdominal pressures may also influence the volume and diameter of the IVC therefore to anticipate measurements at end inspiration and end expiration the maximum and minimum excursion of the diaphragm was used. The IVC diameter was measured 2 cm after the entry to right atrium in all successive scans. As for the echocardiographic scan measures, these reflect the median values between maximal inspiratory and expiratory values in 3 consecutive spontaneous respiratory cycles.

To assess the area and blood flow phase-contrast MRI was performed with velocity encoding magnetic resonance phase-contrast cine pulse sequence (TR, 27 ms; TE, 1.99 ms; Flip angle, 25°; matrix, 256×256; field of view, 320 mm; section thickness, 8 mm, TSENSE rate 2) using retrospective electrocardiogram triggering. The velocity encoding gradient was adjusted to 150 cm/s without aliasing.

Follow up

All 10 study patients were longitudinally followed up for a median period of 55 months (minimum 42 months and maximum 60 months). All patients whilst included in the study had regular yearly clinical follow up where clinical examination was performed and routine bloods (where necessary) were taken. They underwent yearly echocardiography and CMR. Any possible cardiac event was cross verified and recorded.

Statistical Analysis

Statistical analysis was performed using (SPSS). For comparison data between IDIVC and controls we used nonparametric analysis of variance (ANOVA) with subsequent Wilcoxon test. Pairwise comparisons of IDIVC to either baseline or follow up parameters were performed using nonparametric Mann-Whitney test. Level of significance for pairwise comparisons was adjusted for multiple comparisons (p = 0.05; 2 = 0.025). The coefficient of variation for all echocardiographic measurements was 3%.

Reproducibility

All IVC measurements took place at the same beats as per guidelines[2].

Reproducibility of IVC measurements during expiration and inspiration and the collapsibility index for all recordings was analyzed on 2 separate occasions within 14±3 days for intra-observer variability and by a blinded investigator for interobserver variability. These assessments refer to echocardiography. The coefficient of variation for all echocardiographic measurements was 3%. Using Pearson's coefficient a high correlation was found for both intra-observer and interobserver reliabilities (r = .94 and .91, respectively).

Results

During the predefined study period of 4 years we identified 10 patients (5 males and 5 females) with dilated IVC fulfilling the inclusion and after the exclusion criteria. The mean age was 49 years and the median follow up was 55 months.

The initial reason for referral to the echocardiography laboratory is described in Table 1. Three of patients were considered as athletes (cyclists) based on their weekly aerobic activity but the rest were not engaged in any competitive physical activities. The mean IVC diameter dimension as assessed by echocardiography was 33mm in the dilated IVC group in comparison to 18mm in the control group (Table 2). An example of one the study patient's dilated IVC by echocardiography is shown in figure 1a and 1b with and without color doppler respectively. Right heart echocardiographic data is provided in table 3 and CMR data in table 4. A transverse and sagittal orientation of a study patient's dilated IVC by CMR is shown in figures 2a and 2b respectively. Other than IVC measurements the remaining structural measurements between the study group and the control group showed no difference (Tables 2, 3 and 4). IVC measurements were complementary on CMR as with echocardiography as shown in Table 4. There were no differences between echocardiographic and CMR measurements in IVC diameter assessment both at baseline and final visit (Table 2 and Table 4). There was less distensibility seen in the dilated IVC group. The mean IVC area was assessed by CMR (Table 4).

Importantly, over the study period there was no significant progression of IVC in diameter as measured either by echocardiography or CMR. None of the patients suffered any cardiovascular event during the follow up. There were no hospitalizations.

Discussion

Our study, which is the largest contemporary study of IDIVC, adds two important pieces of additional information to the current knowledge of this infrequent disorder. First, that IDIVC could be found in non-athletic individuals and did not relate to sex or age. Second, the degree of IVC dilatation remained unchanged over time without significant progression. Our findings provide further support to the idiopathic and benign nature of this finding.

The IVC is a highly collapsible major vein, and its diameter correlates closely with right side cardiac functions under normal RA pressure, the maximum IVC diameter is less than 22 mm, and the inspiratory collapse is more than 50%. Under high RA pressure, the IVC is dilated (more than 20 mm) and the inspiratory collapse of IVC is diminished. IVC diameter in young, healthy adults, without cardiac pathologic conditions, is frequently above 20 mm commonly regarded as an upper limit of normal and a noninvasive indication of increased right atrial pressure in patients with cardiac or renal disease[6]. Thus, it seems that dilated IVC should not be used as an indicator of increased right atrial pressure in healthy young adults[3].

Idiopathic dilatation of IVC remains a poorly understood, mainly echocardiographic finding usually encountered in young athletes[1]. The finding of dilated IVC seems independent of the type of sport practiced and rather is related to the intensity of training, the number of training hours, which is the only accepted criterion to differentiate between subjects engaged in competitive sports and subjects practicing sport for leisure purposes[1]. In these circumstances it is assumed that this dilation represents a primary IVC adaptation to chronically augmented venous return from the lower part of the body, causing increased volume load with increased cardiac output.

In athletes, other factors may also contribute such as alterations in right ventricular structure due to adaptation and neurohumoral stimuli [1].

Apart from athletes and physically trained subjects, IDIVC can be found in patients without cardiac disease, most of these are isolated case reports[6-8].

Apart from pericardial disease and intrinsic right ventricular disease, the differential diagnosis includes inferior vena cava aneurysms. Those are rare and although the diagnosis of aneurysms are more common in the elderly are associated with an increase in right sided heart pressures, significant TR, and RV dysfunction[4]. In our study we ascertained of the absent structural venous abnormalities by visualizing the entire length of IVC with MRI.

In our study we identified 10 subjects during the 5 years of observation and after meticulous exclusion of alternative causes of dilated IVC. In contrast to prior reports only 3 of the patients could be considered as athletes while the rest were mostly sedentary. This finding along with normal cardiac intracavitary volumes compared to normal volunteers argues against the hypothesis of either increased venous return or cardiac adaptation as cause of dilated IVC. This finding is intriguing and adds to idiopathic nature of this imaging finding. Nevertheless, we found that the overall blood flow through the IVC was marginally albeit statistically significant higher in the dilated IVC group. Perhaps, this may reflect increase blood flow due to larger size vessel. Importantly, we have shown that over time there was no evidence of progressive increase in IVC diameter or area as assessed by both echocardiography and cardiac MRI. Again, this finding is reassuring. Finally, during follow up none of the patients were hospitalized or suffered an adverse cardiovascular event.

There are several limitations to this observational study. First, the highly selective

group of patients leads to inevitable degree of bias of observation. Second, we did not investigate a potential neuro hormonal etiology by blood sampling. Third, we did not assess directly the hematocrit or red cell mass as indirect index of increase blood volume.

Conclusion

In summary, our data suggests that IDIVC is a benign disorder without tendency to progression or increased morbidity. Our findings have implications to reduce implementation of future follow up for these patients as well as providing reassurance.

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Table 1. Characteristics of cohort group with dilated inferior vena cava and reason for baseline echocardiogram

Patient	Reason for Referral	Age (yrs)	Sex	BSA (m^2)	IVC mm
1	Orthopedic Surgery	40	M	1.8	34
2	Exertional Dyspnea	32	F	1.6	33
3	Gallbladder Surgery	43	F	1.6	32
4	Palpitations	31	F	1.4	33
5	Palpitations	32	M	1.8	32
6	Insurance Requirement	42	M	2.0	33
7	Health Assessment	33	F	1.5	32
8	Non-cardiac Chest Pain	35	F	1.6	32
9	Health Assessment	34	F	1.8	31
10	Health Assessment	25	M	1.9	32

M Male and F Female, BSA body surface area, IVC inferior vena cava

Table 2. Parameters of Echocardiography at baseline and follow up of the study population.

Parameters	Study Patients		Control (SD)	*P* Value
	Baseline (SD)	Final Visit (SD)		
SBP, mmHg	130 (7)	131 (4)	129 (5)	ns
DBP, mmHg	72 (5)	73 (5)	73 (4)	ns
Heart Rate, b/min	71 (4)	70 (5)	69 (5)	ns
LVDD, cm	4.5 (0.4)	4.7 (0.3)	4.5 (0.1)	ns
LVSD, cm	2.6 (0.4)	2.8 (0.3)	2.7 (0.3)	ns
IST, cm	0.8 (0.1)	0.8 (0.1)	0.8 (0.2)	ns
PWT, cm	0.8 (0.1)	0.9 (0.1)	0.8 (0.1)	ns
LA, cm	3.3 (0.4)	3.5 (o.4	3.4 (0.5)	ns
LV Mass, g	98 (10)	103 (11)	97 (12)	ns
E, cm/s	91 (16)	86 (15)	85 (10)	ns
A, cm/s	59 (9)	59 (11)	54 (11)	ns
E/A	1.58 (0.3)	1.59 (0.1)	1.58 (0.2)	ns
E' lateral, cm/s	16 (2)	15 (5)	16 (4)	ns
E' Septal, cm/s	11 (2)	12 (4)	11 (2)	ns
IVC, mm	33 (4)	32(4)	18	0.01
IVC collapsibility, %	54 (3)	55 (4)	77 (4)	0.01
Cardiac Output (L)	5.2 (0.5)	5.3 (0.3)	5.3 (0.7)	0.07

SBP indicates systolic blood pressure, DBP systolic blood pressure, LVDD Left ventricular diastolic dimension, LSDD Left ventricular systolic dimension, IST interventricular septal thickness, PWT Posterior Wall Thickness, LA Left atrium, LV Mass Left ventricular Mass, IVC Inferior Vena Cava

Table 3. Right heart data

Parameters	Study patients, n=10		Control, n=10	*P* value
	Baseline	Final Visit		
RA (cm/m^2)	2.5 (0.9)	2.9 (0.7)	2.6 (0.9)	ns
RV diameter (cm)	2.7 (0.9)	2.5 (0.5)	2.6 (0.4)	ns
TAPSE (mm)	1.8(0.4)	1.9 (0.5)	1.7 (0,3)	ns
TR grade	+1	+1	+1	ns
RVSP (mmHg)	18 (2)	20 (3)	18 (3)	ns

RA Right atrium, RV right ventricle, TAPSE tricuspid annular plane systolic excursion, TR tricuspid regurgitation, RVSP right ventricular systolic pressure

Table 4. Parameters of CMR at baseline and follow up of the study population compared to control group.

Parameter	Study patients		Controls	*P* Value
	Baseline	Final Visit		
IVC, mm	33 (3)	32 (4)	17(2)	0.01
IVC blood flow rate, l/min	2.2 (0.4)	2.3(0.5)	2.1 (0.7)	0.04
IVC lumen area, cm^2	2.9 (0.5)	3.0 (0.6)	2.1 (0.4)	0.01
LV Mass, g	95 (5)	103 (4)	98 (10)	ns
EF, %	63 (6)	62 (6)	61 (4)	ns
LVSV, ml	56 (8)	65 (11)	54 (9)	ns
LEDV, ml	99 (3)	103 (4)	100 (4)	ns
LESV, ml	35 (7)	40 (8)	34 (6)	ns
RVEF, %	45 (4)	44 (4)	45 (5)	ns

IVC Inferior Vena Cava, LVSV Left Ventricular Stroke Volume, LEDV Left end ventricular diastolic volume, LVSD Left ventricular systolic volume, LV Mass Left ventricular Mass, Right Ventricular Ejection Fraction

Figure Legends

1. Example of dilated IVC by echocardiography

   1a. Two-dimensional subcostal long axis view

   1b. Colour Doppler of the subcostal long axis view

   IVC indicates Inferior Vena Cava, RA right atrium

2. Example of dilated IVC by CMR

   2a. Transverse SSFP cine of the IVC and aorta

   2b. Sagittal SSFP cine showing the IVC and the aorta

   IVC indicates Inferior Vena Cava, Ao Aorta and SSFP Steady State Free Precession an echo MRI pulse sequence.